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Thermoelectric Cooling for NMR Sample Temperature Control

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This Note is an account of a technique developed to facilitate NMR experiments in a sometimes awkward range of temperatures close to ambient room temperature. Commercially available semiconductor Peltier effect coolers have been applied to control the temperature of the normal air flow into the probe, thus extending downward the usable range of the standard sample temperature controller or providing a new means of temperature control over the limited range used for biological samples in aqueous solution.

In many NMR experiments, sample temperature must be controlled precisely to prevent the deleterious effects of temperature drift. This is an experimental consideration that is of particular relevance to studies in which the solvent or solute exhibit temperature-dependent resonance shifts, thus is of primary importance in the study of aqueous solutions. Temperature instability is known to contribute to t_1 or t_2 noise in multidimensional NMR experiments (*1*) and to increase subtraction artifacts in difference spectroscopy (*2*). While several methods have been aimed at improving the accuracy of temperature measurement (*3* and references therein), there has been no fundamental improvement or simplification in the manner in which the desired temperatures are obtained. Usually, air is passed round the sample tube after passing an electrical heating element, and a feedback system regulates the temperature of the air by controlling the power fed to the heater. This system cannot yield sample temperatures less than the equilibrium temperature of the probe, which may be some degrees warmer than the room, and is generally not very satisfactory at temperatures within a few degrees of this equilibrium temperature. The minimum temperature for stable regulation may therefore be up to 10°C above room temperature.

Lower temperatures can be achieved by precooling the air, or by replacing it with freshly evaporated nitrogen, and then using the standard control system to reheat it to the required temperature. Within the probe, the precooled air passes through a considerable length of tubing before it reaches the sample. In doing so, there may be significant rewarming. We find that air entering the probe at −20°C may have warmed to +4°C before leaving the dewared section that contains the heater. In order to obtain a given reduction in sample temperature, the air entering the probe must be precooled by a much greater amount. This may be achieved by passing the air through a coiled tube immersed in a suitable liquid which is cooled by the addition of ice or solid carbon dioxide. The coolant needs repeated replenishing for experiments of any length, and the continuous use of cryogens can become expensive. A refrigerated ‘‘cold finger’’ may be used to cool the cold bath and purpose-built refrigeration systems are commercially available but are bulky and expensive. We have developed a system for sample temperature control over the approximate range 5–50°C by cooling (or warming) the air stream into the probe with the use of thermoelectric ‘‘refrigeration.’’ The hardware is inexpensive, requires essentially no maintenance, is convenient to the instrument operator, and can be coupled to commercially available probes without the need for further modifications.

Initial development was carried out in one laboratory (Dyson Perrins, Lab-1), a chemical laboratory where it is necessary to be able to perform many experiments at ambient temperature but also over the range from −100 to +100°C in many solvents. A slightly different approach has been adopted in a collaborating laboratory (Biochemistry Dept., Lab-2), which deals solely with biological samples in aqueous solutions and therefore works principally in the range 5–50°C. To satisfy their different requirements, the two laboratories have developed slightly different thermoelectric cooling systems. Six cooler installations are in routine use. The devices constructed in the two laboratories take the same general form. A small unit (the ‘‘cooler’’) adjacent to the air connection into the probe contains the thermoelectric cooler (TEC) (*4*) and two heat exchangers. Dry air passes through a labyrinth of small passages in a metal block clamped to the cold side of the TEC before passing into the probe. On the other side of the TEC, a larger metal plate is

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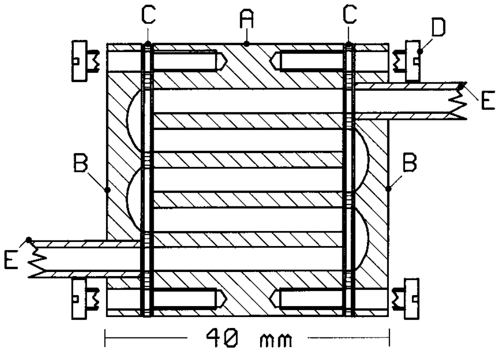

FIG. 1. Air heat exchanger: A metal block (A), 40 × 36 × 6 mm thick, has 3.5 mm diameter passages drilled across its width. These are linked into a continuous air passage by end caps (B) and gaskets (C), held in position by 3 mm screws (D). Air inlet and outlets are tubes (E). The assembled heat exchanger is 40 × 40 mm to fit the active surface of the thermoelectric cooler.

cooled by a flow of water which removes the heat pumped from the air and also the heat generated by the electrical power dissipated in the TEC. The water is recirculated by a pump, situated away from the magnet, through an air-cooled device which keeps the water temperature within a few degrees of the ambient room temperature. Electrical power is supplied to the TEC by an electronic power supply unit (psu) which may be coupled to a temperature controller.

The cold-side heat exchangers used in Lab-1 are shown in Fig. 1. The material used was aluminum but copper would have some advantages. In order to improve thermal contact between the gas and the metal, spiral baffles of thin metal strip were inserted into each of the gas passages. Note that the gas supply must be dry enough for its dew point to be below the minimum temperature encountered in the heat exchanger, about −25°C, to avoid ice formation and consequent blockage. On the ‘‘hot’’ side of the TEC, the water-cooled heat sink must be designed to be compatible with the circulating pump. The most readily available pumps giving adequate water flow are those supplied for domestic central-heating systems (*5*). As central-heating pumps work best with larger flow rates than are strictly necessary for this purpose, it is advisable to use large bore piping and to avoid narrow constrictions. Given the use of large water flow, the detailed design of the heat sink is not critically important. The main problem is to make it reliably leak free and to avoid turbulence that could transmit vibration to the probe. In a successful design in Lab-1, a semiconductor heat sink (*6*) forms the upper surface of a closed box machined from aluminum. Water enters and leaves through 10 mm bore pipes and is directed to flow between the fins by 4 mm holes in the sides of the pipes. The maximum recommended operating temperature for the TEC is 85°C. When reversing the current to heat, rather than cool, the safe temperature can easily be exceeded. Also, failure of the water supply can lead to a potentially excessive temperature rise. To guard against these eventualities, thermal limit switches (*7*) have been included in the assembly. One, opening at 80°C, on the outer surface of the gas heat exchanger and the other, opening at 50°C, on the water-cooled sink close to the TEC. These are connected electrically in series and to a relay in the psu. In Lab-2, the water-cooled heat sink also includes air-cooling fins which would limit the temperature rise in case of water circulation failure.

The water-cooled heat sink makes a convenient platform upon which to mount the TEC and the gas-side heat exchanger. In clamping them together, the TEC suppliers recommend the use of considerable pressure, but it is necessary to ensure that the clamping components do not form a heat shunt between the hot and cold sides. It is also necessary to insulate the cold side from convective heat transfer and from condensation. A solution shown in Fig. 2 is to form a partial outer casing from sheet aluminum, inserting a spacer between this and the gas heat exchanger, and clamping the casing with bolts to the water-cooled heat sink. The spacer is machined from a dimensionally stable plastic (*8*) and is designed with a minimum cross-sectional area consistent with the pressure to be exerted and with the maximum length of heat-transfer path allowable for access to the probe. The casing deforms elastically as the clamping bolts are tightened, thus ensuring that the pressure is maintained despite thermal movements and deformation of the other components. The space between the casing and the heat sinks was

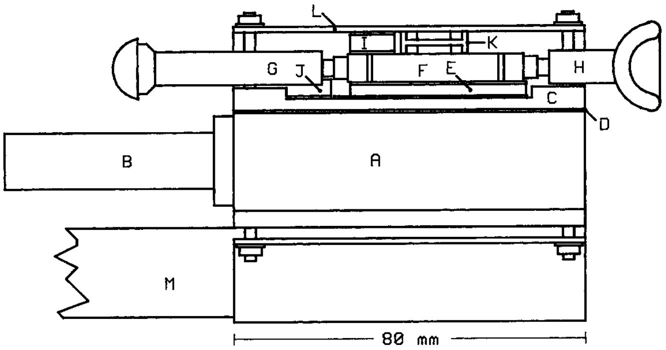

FIG. 2. The cooler assembly includes the main body of the water-cooled heat sink (A) with water inlet and exit pipes (B), the upper plate of the heat sink (C), and a sealing gasket (D). On these are mounted the thermoelectric cooler (E) and the air heat exchanger (F) with its inlet and outlet pipes (G, H) and the over-temperature cut-out switches (I, J). Mechanical pressure is applied through the spacer (K) by the metal plate (L) which forms the top and two sides of the assembly. The whole is mounted on a supporting rod (M). The gaps between components (A) and (L) are filled with foamed RTV silicone compound which is trimmed off flush at the open ends of the assembly. The length of the assembly, including the air and water pipes but not including the supporting rod, is 150 mm. The basic width is 68 mm, and including the electrical connector, it is 88 mm. The height is 46 mm, or 70 mm including the supporting rod.

filled, after assembly, with a foaming silicone preparation (*9*). This formed a barrier to condensation and provided good thermal insulation. A socket for electrical connections was mounted on the outside of the casing. In Lab-1, the coolers are fitted with glass connectors that are compatible with the standard probe air inlet, thus permitting them to be connected into the probe air supplies when required.

The water-cooling circuits in Lab-1 include flexible piping from the coolers to demountable connectors (*10*) close to the magnet bases. The rest of the water circuit is constructed from domestic central-heating components. The pump circulates water through standard 15 mm copper piping and a pressed steel radiator (*11*). A 1 liter plastic bottle serves as a header tank and the water contains a corrosion inhibitor (*12*). In Lab-2, it is found that the whole temperature range required can be achieved with thermoelectric devices without using heaters in the probes. To take advantage of this, the probes have been fitted with dewars of a modified design. The new dewars have a narrow center tube, increasing the gap in the vacuum jacket, decreasing the residence time of the flowing gas, and reducing the contact area with the gas. A significant extension of the operating temperature range is achieved. The coolers are permanently installed on mounting plates at the base of the magnets. Microbore tubing connects the coolers directly to the electronic control modules which contain similar pumps and header tanks, but, instead of the radiators, copper coils are mounted in the air flow from fans which also cool the electronic components.

A power supply unit and temperature controller is available commercially (*13*) but both laboratories have used in-house developments for this purpose. In Lab-1, different electronic equipment has been fitted to spectrometers of different generations. Most simply, power is supplied to the cooler from a stabilized power supply at a constant current of up to 6 A. The original temperature control system is left unmodified. The cooler simply serves to reduce the equilibrium temperature of the sample in the probe and hence to extend downward the routinely available temperature range of the existing temperature controller. It is, however, fitted with a relay circuit to interrupt the power supply if the water circulation fails or the cooler otherwise overheats. In another installation, the original temperature controller (*14*) has been modified and now optionally supplies a signal to a purpose-built psu to control the current supplied to the cooler, hence including it within the control loop. This supply can reverse the current through the TEC, hence permitting control both below and above the equilibrium temperature. In Lab-2, temperature control using only the TEC has been adopted as standard. Commercially available PID controllers (*15*) are coupled to psu's of in-house design to give control over the whole temperature range normally used in that laboratory.

The coolers achieve a reduction of temperature of the air entering the probes of approximately 40°C. Where it is necessary to achieve lower temperatures, it is possible to reduce the gas temperature by about a further 12°C by adding a second TEC (*16*) between the first and the gas heat exchanger, driving this with up to one-third of the current of the first. It has not been found necessary to use the second TEC here.

Thermal performance varies markedly between probes, making it difficult to specify the results to be expected with any randomly selected probe. In Lab-1, the coolers are now used in routine work to keep the sample temperature close to room temperature, which is controlled at about 22°C, thus permitting rapid equilibration of the sample temperature in the probe and reducing the working temperature by about 10°C. When necessary for specific experiments the temperature may be adjusted rapidly with a range of a few degrees and may be reduced to a minimum of about 10°C, increasing the gas flow as necessary to achieve this. Enhanced results are obtained from experiments such as steady-state NOE difference measurements where subtraction of almost equal spectra can lead to significant errors in the presence of temperature instability. In Lab-2, the new dewars give the advantage of being able to cool further. The method described is found to be particularly well suited to study of biological macromolecules where stable temperature control within a limited range (approximately 5–50°C) is required and is achievable by this technique. Considerable economy in the use of refrigerants has been achieved and replenishment of cold baths is no longer required.

In summary, we have described a new method for sample temperature control in the range 5 to 50°C that is inexpensive to install and to operate, simple to use, and compatible with commercial instruments. This proves to be beneficial with the wide ranging work of an organic chemistry laboratory and particularly so in a laboratory specializing in the study of biological macromolecules in aqueous solution.

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4. DuraTEC Thermoelectric Cooler, Model DT12-8, (40 mm square, 70 W max.). Marlow Industries Europe, 7 Laura House, Jengers Mead, Billingshurst, West Sussex, RH14 9NZ, UK.

5. For example, Grundfoss Selectric Domestic Circulator, local plumbers' suppliers.

6. Heatsink 2E, Part HQ70M, MPS, P.O. Box 777, Rayleigh, Essex SS6 8LU, UK.
7. Bimetallic TO-220, AIRPAX, Supplied by Farnell Electronic Components Ltd., Canal Road, Leeds LS12 2TU, UK.
8. Glass-Filled Nylon 66, RS Components Ltd., P.O. Box 99, Corby, Northants, NN17 9RS, UK.
9. Firestop 3-6548 Silicone RTV Foam, RS Components Ltd., P.O. Box 99, Corby, Northants, NN17 9RS, UK.
10. Polypropylene Quick Couplings, RS Components Ltd., PO Box 99, Corby, Northants, NN17 9RS, UK.
11. Radiator minimum area 0.4 m^2, e.g., 600 × 700 mm. Local plumbers' suppliers.
12. Fernox, COPAL, Local plumbers' suppliers.
13. Marlow Industries, 7 Laura House, Jengers Mead, Billingshurst, West Sussex, RH14 9NZ, UK.
14. Bruker, VT-1000.
15. Controller/Programmer 815/818, Eurotherm Ltd., Unit 8, Sackville Road, Hove, East Sussex, BN3 7AN, UK.
16. Marlow Industries, Model MI 1069T, 40 mm square, 50 W max.